泽布替尼单药治疗华氏巨球蛋白血症（WM）的 3 年随访研究。

Three-year follow-up of treatment-na ıve and previously treated patients with Waldenstro m macroglobulinemia(WM) receiving single-agent zanubrutinib.

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背景：

布鲁顿酪氨酸激酶（BTK）抑制剂已在 WM 患者中的疗效已得到验证。泽布替尼是一种有效的高选择性的 BTK 抑制剂，一项 1/2 期研究中对其治疗初治（TN）和复发/难治（R / R）WM 患者进行了评估。

方法：

研究者纳入 TN 或 R / R WM 患者，并根据国际 WM 研讨会（IWWM）标准进行治疗。治疗方案为口服泽布替尼，每次 160 mg，BID（n = 50）或每次 320 mg，QD（n = 23），直至疾病进展或出现不可接受的毒性。疗效终点包括根据 IWWM-6 标准达到完全缓解（CR）或非常好的部分缓解（VGPR）的患者比例 73 名可评估患者（24 TN，49 R / R）参与疗效分析。

结果：

在 2014 年 9 月至 2018 年 8 月之间，共有 77 名 WM 患者（24 TN 和 53 R / R）接受泽布替尼治疗（55％患者的年龄大于 65 岁； 21％患者的年龄大于 75 岁）。中位随访时间为 32.7 个月，此时仍有 73％的患者接受治疗。 中止治疗的原因包括不良事件（AE）[13％（只有一种相关）]、疾病进展（10.4％）和其他（3.9％）。患者的总有效率为 **96％**，VGPR / CR 占有效人群的 **45％**；这个比率随时间推移而增加：在 6 个月时占 22％，在 12 个月时占 33％，在 24 个月时达到 45％。三年无进展生存期（PFS）为 81％，总生存率（OS）为 85％。最常见的 AE 是上呼吸道感染（52％）、挫伤（33％，均为 1 级）和咳嗽（22％）。最值得留意的 AE 包括中性粒细胞减少症（18.2％）、严重出血（4％）、房颤/扑动（5％）和 3 级腹泻（3％）。

结论：

继续使用泽布替尼进行治疗的长期随访研究表明，在大多数 WM 患者中，泽布替尼的缓解质量高且持久。长期治疗会增加 VGPR / CR 率。疾病进展并不常见。长期使用泽布替尼治疗这些患者的安全性是可以接受的。

原文摘要：

Abstract

Background: Inhibitors of Bruton tyrosine kinase (BTK) have established therapeutic activity in patients with WM. Zanubrutinib, a potent and selective BTK inhibitor was evaluated in a phase 1/2 study in treatment-na ıve (TN) and relapsed/refractory (R/R) patients with WM.

Methods: Patients had TN or R/R WM and required treatment as per International Workshop on WM (IWWM) criteria. Treatment consisted of oral zanubrutinib at 160 mg twice daily (n = 50) or 320 mg once daily (n = 23) until disease progression or unacceptable toxicity. Efficacy endpoints included the proportion of patients achieving a complete response (CR) or very good partial response (VGPR) in accordance with IWWM-6 criteria. Efficacy analyses were conducted on the 73 patients evaluable (24 TN, 49 R/R).

Results: Between September 2014 and August 2018, 77 patients with WM (24 TN and 53 R/R) began treatment with zanubrutinib (55% aged . 65 years; 21% aged . 75 years). At a median follow up of 32.7 months, 73% remain on treatment. Reasons for treatment discontinuation included adverse events (AE) in 13% (only one related), disease progression (10.4%), and other (3.9%). Results are presented for TN and R/R combined. The overall response rate was 96% and VGPR/ CR rate was 45%. The rates of VGPR/CR increased over time; 22% at 6 mos, 33% at 12 months and 45% at 24 months. Three-year progression-free

survival (PFS) was 81%, and overall survival (OS) was 85%. The most commonly reported AEs were upper respiratory tract infection (52%), contusion (33%, all grade 1) and cough (22%). AEs of interest include neutropenia (18.2%), major hemorrhage (4%), atrial fibrillation/flutter (5%), and grade 3 diarrhea (3%).

Conclusions: Long-term follow up with continued zanubrutinib treatment demonstrated deep and durable responses in the majority of WM patients. The rates of VGPR/CR increased with prolonged therapy. Disease progression was uncommon. The safety profile of long-term zanubrutinib therapy in these patients was tolerable. Clinical trial information: NCT02343120. Research Sponsor: BeiGene.

参考文献：

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